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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/531,369	03/21/2000	Mark Williamson	07334-122001	6489

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EXAMINER
CANELLA, KAREN A

ART UNIT	PAPER NUMBER
1642	15

DATE MAILED: 03/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/531,369	Williamson
Examiner	**Art Unit**
Karen Canella	1642

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above, claim(s) *4-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 21, and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some* c)☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)

16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18)☐ Interview Summary (PTO-413) Paper No(s). _____

19)☐ Notice of Informal Patent Application (PTO-152)

20)☐ Other:

DETAILED ACTION

1. The finality of the Office action of Paper No. 13 has been vacated. Newly submitted claims 4 and 5 have been renumbered as claims 21 and 22 pursuant to Rule 1.26. Claims 1-22 are pending. Claims 4-20 remain withdrawn from consideration. Claims 1-3, 21 and 22 are under consideration.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New Grounds of Rejection

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 22 recites MDA-0 which is not defined in the specification or known in the art. For purpose of examination, the instance of MDA-0 will be read as MDA-9.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

6. Claims 1-3, 21 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Fischer (US 6,071,696) as evidenced by Serrone et al (Melanoma Research, 1999, Vol. 9, pp. 51-58).

Claim 1 is drawn to a method for determining whether a test compound is a candidate modulator of drug resistance comprising determining the level of MDA-9 expression in the cell in

the presence or absence of the test compound , wherein a compound is identified as a candidate modulator if the level of expression of MDA-9 differs in the presence or absence of said compound. Claim 2 embodies MDA-9 as encoded by an endogenous gene. . Claim 21 embodies determining the level of expression of MDA-9 by measuring the level of expression of MDA-9 mRNA. Claim 22 embodies determining the level of expression of MDA-9 by measuring the level of expression or MDA-9 protein.

Fischer discloses a method of identifying compounds capable of inducing terminal differentiation in cancer cells comprising incubating cancer cells with a test compound and measuring the expression of MDA-9, the reduced expression of MDA-9 in the presence of the test compound indicating that the compound is a candidate for an inducer of terminal differentiation. Fischer discloses the detection of MDA-9 levels as both the detection of MDA-9 mRNA (column 14, lines 16-29) and the detection of MDA-9 protein (column 10, lines 3-4) Fischer discloses MDA-9 as the melanoma differentiation associated gene which is an endogenous gene. Fischer does not specifically disclose that compounds which induce terminal differentiation and decreased expression of MDA-9 in cancer cells will be the same as candidate modulators of drug resistance in cancer cells, however, the claimed method of selecting for candidate compounds which modulate the drug resistance of the cell would be inherent in the method disclosed by Fischer as both the claimed method and disclosed method rely on the ability of test compounds to modulate the level of MDA-9. Further, Serrone et al disclose that malignant melanoma cells are drug resistant. Therefore, the induction of decreased expression of MDA-9 in melanoma cells would be commensurate with a decreased level of drug resistance in said cells.

7. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 3 is drawn to a method for determining whether a test compound modulates drug resistance

of a cell comprising incubating MDA-9 protein in the presence of a test compound, determining whether the test compound binds to the MDA-9 protein, administering a test compound which binds to MDA-9 to a non-human mammal having drug resistant cells, wherein the test compound is identified as a modulator of drug resistance if the drug resistance of the cells are altered. The specification does not teach a specific part of MDA-9 that should be bound by the target compound. The specification teaches that MDA-9 is identical in amino acid sequence to syntenin. Grootjans et al teach that syntenin is another name for the syndecan cytoplasmic link protein (sycl) or syndecan interacting protein. Grootjans et al teach that syntenin self-interacts as well as interacts with other proteins through two PDZ domains and the N-terminal domain. Grootjans et al conclude that the molecular associations of syntenin are determined by complex intra- and inter-molecular interactions. Grootjans et al further teach that different conformations of syntenin directly or indirectly associate with both microfilaments and microtubuli and that syntenin functions as an adaptor molecule to link syndecans and other molecules to the cytoskeleton. Given the teachings of Grootjans et al, one can conclude that the conformation of MDA-9 has bearing on activity of the MDA-9 protein, as only certain "pools" of syntenin are able to interact with microfilaments and microtubuli (page 22, lines 3-9). The specification does not teach a conformation of MDA-9 that would be commensurate with drug resistance in a cell. Therefore one of skill in the art would be subject to undue experimentation in order to find a candidate modulator binding to MDA-9 having the conformation which would be active in drug resistant cells as the specification does not teach how to conserve this conformation in vitro. Further, as Grootjans et al teach that the interaction of syntenin with other proteins may require oligomerization of both syntenin and the interacting protein (page 19, lines 6-10) and that syndecans in addition to several, but not all proteins terminating with t-FXA may be compete with syndecans for syntenin (page 19, lines 22-24). Given the lack of teachings regarding the conformation of the MDA-9 (syntenin) protein and the unreliability of the art with regard to knowledge of the binding partners of MDA-9, mode of binding to MDA-9 (monomer or

oligomer) and the lack of teaching in the specification regarding the precise locations in the amino acid sequence of MDA-9 which dictate binding to MDA-9, one of skill in the art would be subject to undue experimentation in the screening of agents which bind to MDA-9 as candidate test compounds.

8. All other rejections and objections as stated in Paper No: 13 are withdrawn.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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TECHNOLOGY CENTER 1600

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
March 1, 2002